REMARKS

Claims 7-20 are pending in the application, claims 1-6 having been cancelled without prejudice. Claims 7-10 and 12 have been amended to change their dependency from claim 1, which has been cancelled, to independent claim 13. Support for the amendments can be found in the specification at, e.g., page 3, line 28, to page 4, line 23. No new matter has been added by these amendments.

35 U.S.C. § 102(e)

On page 2 of the Office Action, the Examiner rejected claims 1 and 2 as allegedly anticipated by Lynch et al., U.S. Patent No. 5,830,469 ("Lynch"). Claims 1 and 2 have been cancelled, thereby obviating the rejection. Accordingly, applicants request that the Examiner withdraw the rejection.

35 U.S.C. § 103(a)

On pages 2-3 of the Office Action, the Examiner rejected claims 5-12 as allegedly unpatentable over Lynch. Claims 5 and 6 have been cancelled, thereby obviating the rejection of these claims. Claims 7-12 have been amended to depend from independent claim 13, which is not rejected under this heading. Accordingly, applicants request that the Examiner withdraw the rejection.

On pages 3-4 of the Office Action, the Examiner rejected claims 1, 2, and 4-20 as allegedly unpatentable over Hattori et al. (1998) Blood 91:4051 ("Hattori") in view of Lynch. The Examiner stated that "Hattori et al. teach a method of treating a subject having GVHD, using a composition comprising antibodies to Fas ligand." As acknowledged by the Examiner, "[t]he claimed invention differs from the Hattori et al. disclosure in that it [Hattori] teaches administration of anti-Fas *ligand* antibodies, and does not teach or suggest administration of anti-Fas antibodies." However, according to the Examiner,

> [i]t would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the antibodies of Lynch et al. in the method

of Hattori et al. for the treatment of GVHD. One of skill in the art would have been motivated to do so, and would have expected success, in view of Lynch's teaching of the equivalence of anti-Fas Ligand and Anti-Fas antibodies for the blocking of signaling via FAS.

Applicants respectfully traverse the rejection in view of the claim amendments and the following comments.

Claims 1, 2, and 4-6 have been cancelled, thereby obviating the rejection of these claims. Claim 13, the independent claim rejected herein, is directed to a method of treating a subject having graft-versus-host-disease (GVHD) by administering to the subject a composition containing anti-Fas antibodies in an amount effective to inhibit binding of Fas ligands to Fas receptors in the subject. Claims 7-12 have been amended to depend from claim 13.

Hattori describes the effects of the administration of neutralizing anti-Fas ligand (FasL) and/or anti-TNFα monoclonal antibodies in a mouse model of GVHD. Hattori concludes that either monoclonal antibody alone delays mortality and improves body weight in the mouse model, whereas administration of both antibodies results in a complete protection from GVHD. However, and as acknowledged by the Examiner, Hattori does not teach or suggest methods of treating GVHD by administration of anti-Fas antibodies.

Lynch does not add what Hattori is lacking. Lynch not only fails to suggest that anti-Fas antibodies can be used to treat GVHD, it actually teaches away from using anti-Fas antibodies in such a treatment method. According to Lynch, GVHD is an example of a disease in which it is desirable to promote activated-induced cell death (AICD) of T cells (column 15, lines 21-29). Accordingly, Lynch describes treating GVHD by administering TNFα *in vivo*, thereby promoting apoptosis of T lymphocytes that play a role in causing the disease. Lynch nowhere describes treating GVHD by inhibiting apoptosis and/or by administering anti-Fas antibodies to a subject. Lynch's method of treating GVHD is therefore in direct contrast to that of the claimed invention, which entails administering to a subject anti-Fas antibodies that prevent the binding of Fas-ligands to Fas receptors, thereby inhibiting apoptosis.

In light of the above, applicants respectfully submit that the cited references would not have supplied the skilled artisan, at the time of the filing of the present application, with the

requisite suggestion and motivation to use anti-Fas antibodies in a method of treating GVHD. Accordingly, applicants request that the Examiner withdraw the rejection.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are now in condition for allowance, which action is requested.

Attached is a marked-up version of the changes being made by the current amendments. The attached page is captioned "Version with Markings to Show Changes Made." Also attached is a listing of the claims pending upon entry of the amendments presented herein.

Enclosed is a Petition for One Month Extension of Time and a check for the extension fee. Please apply any other charges (or credits) to Deposit Account No. 06-1050, referencing Attorney Docket No. 11141-003001.

Respectfully submitted,

Date: February 7, 2003

Jack Brennan
Reg. No. 47,443

Fish & Richardson P.C.
45 Rockefeller Plaza, Suite 2800
New York, New York 10111
Telephone: (212) 765-5070
Facsimile: (212) 258-2291

Version with Markings to Show Changes Made

In the Claims:

Claims 1-6 have been cancelled without prejudice.

Claims 7-10 and 12 have been amended as follows:

7. (Amended) The method of claim 14 [5], wherein the composition contains a level of anti-Fas antibodies sufficient to inhibit at least 40 percent of FasL binding to Fas receptor.

8. (Amended) The method of claim 14 [5], wherein the composition contains a level of anti-Fas antibodies sufficient to inhibit at least 50 percent of FasL binding to Fas receptor.

9. (Amended) The method of claim 14 [5], wherein the composition is administered at a dosage of at least 0.1 g/kg/day.

10. (Amended) The method of claim 14 [5], wherein the composition is administered by infusion.

12. (Amended) The method of claim 13 [4], wherein the composition is administered by infusion at a dosage of at least 0.75 g/kg/day.

Pending Claims

7. The method of claim 14, wherein the composition contains a level of anti-Fas antibodies sufficient to inhibit at least 40 percent of FasL binding to Fas receptor.

8. The method of claim 14, wherein the composition contains a level of anti-Fas antibodies sufficient to inhibit at least 50 percent of FasL binding to Fas receptor.

9. The method of claim 14, wherein the composition is administered at a dosage of at least 0.1 g/kg/day.

10. The method of claim 14, wherein the composition is administered by infusion.

11. The method of claim 10, wherein the composition is administered at a dosage of at least 0.1 g/kg/day.

12. The method of claim 13, wherein the composition is administered by infusion at a dosage of at least 0.75 g/kg/day.

13. A method of treating a subject having graft-versus-host-disease (GVHD), the method comprising administering to the subject a composition comprising anti-Fas antibodies in an amount effective to inhibit binding of Fas ligands to Fas receptors in the subject.

14. The method of claim 13, wherein the composition comprises an intravenous immunoglobulin (IVIG) mixture.

15. The method of claim 14, wherein the IVIG is of human origin.

16. The method of claim 14, wherein the IVIG contains an anti-Fas antibody at a concentration of at least 0.1 mg/ml.

17. The method of claim 14, wherein the IVIG contains an anti-Fas antibody at a concentration of at least 8 mg/ml.

18. The method of claim 13, wherein the composition comprises an anti-Fas antibody and is administered at a dosage of at least 0.1 mg/kg/day for at least two days.

19. The method of claim 14, wherein the IVIG is administered at a dosage of least 0.1 g/kg/day for at least two days.

20. The method of claim 14, wherein the IVIG is administered by infusion at a dosage of 0.75 g/kg/day for four consecutive days.